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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,157	05/01/2001	Michael D. Smith	0942.5040001/RWE/MTT	2674

26111 7590 05/10/2004

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 05/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/845,157	SMITH ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-4,7-29,44-47,51 and 52* is/are pending in the application.

4a) Of the above claim(s) *4,8,9,19-23,25 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,7,10-18,24,26-28,44-47,51 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status

1. Claims 2-4,7-29,44-47,51 and 52 are pending.

Claims 2,3,7, 10-18, 24, 26-28, 44-47,51 and 52 are rejected.

Claims 4,8,9,19-23,25 and 29 are withdrawn from consideration.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Claim Interpretation

2. The claims, as most recently amended, now require a substitution of, for example, a Leucine at position 52 for a different amino acid. However, so long as the amino acid at position 52 of the reverse transcriptases cited is not leucine, it will meet the claim since it will be "substituted" from a leucine. In a product claim, there is no structural difference between a reverse transcriptases which naturally has a substitution at position 52 or one which is altered by mutation to have a substitution at position 52.

Further, with regard to the term "retroviral", upon which Applicant places much weight, there is no structure or definition to support that weight. The specification lists a variety of different retroviral reverse transcriptases (see pages 3 and 4), but never, in the extensive definitions section beginning at page 20, defines the term "retrovirus". The specification does indicate that Taq is a reverse transcriptase (see page 32).

Finally, no structure is imposed by the term "wild type retroviral reverse transcriptases" since no specific structure or specific definition is given for this term in the specification.

Claim Rejections - 35 USC § 112, second paragraph

3. Claims 16-18 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. In some of the dependent claims, such as claim 16, the claim says the RNAse H activity, for example, is reduced in comparison to the corresponding wild-type enzyme. However, given the breadth of claim 2, it is vague and indefinite what constitutes the "corresponding wild type enzyme". That is, since there is no fixed structure for the claimed reverse transcriptase, it is indefinite what structure should be compared to the claimed reverse transcriptases for purposes of being "wild type". Therefore, for purposes of prior art, any prior art enzyme may be deemed wild type.

Claim Rejections - 35 USC § 112 – Written Description

5. Claims 2, 3, 7, 10-18, 24, 26-28, 44-47, 51 and 52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed

by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID Nos. As discussed above, the claims essentially read on any reverse transcriptases whatsoever. There is no description in the specification of any MMLV reverse transcriptases which differ in sequence from the known prior art sequence. Also, claim 49, which is drawn to particular positions, clearly reads on any reverse transcriptase from any organism without the sequences of those enzymes being taught or suggested in the specification. Further, the claim permits any number of mutations except the specifically excluded position 223 mutation. The broadest claim is drawn to any reverse transcriptase from any species with any sequence and any mutation. Thus the claims encompass a genus which comprises hundreds of millions of different possibilities since in a protein of about 671 amino acids there are more than 671^{19} possible single amino acid changes (this equates to about 5×10^{53} different possibilities). The number of possible changes becomes even more astronomical if multiple amino acid changes are permitted. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains are required. No structural limitations or requirements which provide guidance on the identification of sequences which meet the functional

limitation of enhanced thermostability is provided. Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, proteins which have a removable amino terminal end, while only specific amino acid sequence variants have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence have been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the thermostable MMLV reverse transcriptases lack any specific structure, which is precisely the situation of naming a type of material which is generally known to likely exist, but, except for the wild type protein with the exemplified mutations, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to any reverse transcriptase which is modified for enhanced thermostability. In particular, while some claims define

particular amino acids, such as the H204R change, the entire surrounding sequence of 600 amino acids is not defined in these claims, leaving only the particular change as a fixed point in what can be a protein of any sequence.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a reverse transcriptase with enhanced thermostability, without sufficient structure to meet this functional limitation.

In the instant application, certain specific SEQ ID NOs are described implicitly, though not explicit teaching of the complete sequence of a particular MMLV reverse transcriptase is found in the specification. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise the wild type MMLV reverse transcriptase as shown by the

prior art sequence modified at the selected positions as having enhanced thermostability. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. As discussed above under claim interpretation, the claim simply requires that one of the cited positions be changed in some way. The references which follow each change at least one of the four cited positions in some way.

8. Claims 2, 16-18, 24, 26, 27 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Blain et al (J. Biol. Chem. (1993) 268(31):23585-23592).

Blain et al teach altered MMLV reverse transcriptases which have expressly shown reduced RNAse H activity (see page 23588, table 1), retain DNA polymerase activity (see page 23588, table 1) and discusses that some fragments are inactive (see page 23591, column 2, last paragraph). Thus, relative to completely inactive fragments, the mutant MMLV reverse transcriptases shown by Blain have increased fidelity and thermostability while they have reduced RNAseH activity relative to wild type MMLV reverse transcriptase. Blain specifically teaches the delta101 mutation, which removes

all the amino acids from positions 213-313, which would include the methionine at position 289 and the threonine at position 306 (see page 23586, column 1).

9. Claims 2, 12-18, 24 and 26-28 are rejected under 35 U.S.C. 102(a) as being anticipated by Arakawa et al (JP 2000-139457, published May 23, 2000).

Arakawa et al teach altered MMLV reverse transcriptases which have expressly shown reduced RNAse H activity (see translation, page 2 of 9, paragraph 0008) which retains enhanced DNA polymerase activity (see translation, page 2 of 9, paragraph 0009) and expressly teaches thermostability at 60 C of the modified enzyme which retains significant activity at 60 C (see abstract and translation, page 6 of 9). Further, as a review of the sequence of Arakawa shows (see page 9-10 of Japanese text), amino acid 52 is proline, not leucine. Further, the amino acid at 204 is Leucine, not histidine, and the position at 289 is valine and the position at 306 is Glycine. Thus, Arakawa teaches modifications at each of the cited positions.

10. Claims 2, 12-18, 24 and 26-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Lawyer et al (J. Biol. Chem. (1989) 264(11):6427-6437).

Lawyer teaches a Taq polymerase enzyme which inherently has RNAse H activity and which expressly teaches thermostability at 60 C of the modified enzyme which retains significant activity at 60 C (see figure 2). This enzyme represents a "modified" MMLV reverse transcriptases, where many positions are "modified" and where position 204 is not histidine, position 306 is not threonine and position 289 is not methionine. Therefore, this protein anticipates the claim as it is currently broadly claimed. With regard to the term "retrovirus", which is a source indicator, it has no

structural impact on the protein, and therefore simply represents a non limiting element of a preamble.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 44-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Blain et al or Arakawa et al or Lawyer et al, either in view of Stratagene Catalog (1988) p. 39.

Blain et al teach altered MMLV reverse transcriptases which have expressly shown reduced RNAse H activity (see page 23588, table 1), retain DNA polymerase activity (see page 23588, table 1) and discusses that some fragments are inactive (see page 23591, column 2, last paragraph). Thus, relative to completely inactive fragments,

the mutant MMLV reverse transcriptases shown by Blain have increased fidelity and thermostability while they have reduced RNAseH activity relative to wild type MMLV reverse transcriptase. Blain teaches adding nucleotides and primers (see page 23586, column 2).

Arakawa et al teach altered MMLV reverse transcriptases which have expressly shown reduced RNAse H activity (see translation, page 2 of 9, paragraph 0008) which retains enhanced DNA polymerase activity (see translation, page 2 of 9, paragraph 0009) and expressly teaches thermostability at 60 C of the modified enzyme which retains significant activity at 60 C (see abstract and translation, page 6 of 9). Arakawa teaches the use of RT's in RT-PCR (see page 1 of 9 of translation).

Lawyer teaches a Taq polymerase enzyme which inherently has RNAse H activity and which expressly teaches thermostability at 60 C of the modified enzyme which retains significant activity at 60 C (see figure 2). This enzyme represents a "modified" MMLV reverse transcriptases, where many positions are "modified" and where position 204 is not histidine, position 306 is not threonine and position 289 is not methionine. Therefore, this protein anticipates the claim as it is currently broadly claimed. With regard to the term "retrovirus", which is a source indicator, it has no structural impact on the protein, and therefore simply represents a non limiting element of a preamble.

Neither Blain nor Arakawa nor Lawyer teach formation of a kit with these known reagents.

Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method and products of either Blain or Arakawa into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantitites of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantitites you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control" (page 39, column 1).

New Grounds of Rejection necessitated by Amendment

Claim Rejections - 35 USC § 112 – New Matter

14. Claims 2, 3, 7, 10-18, 24, 26-28, 44-47, 51 and 52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention.

As MPEP 2163.06 notes " If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

Here, the new limitation to claim 2 which states "wherein the retroviral reverse transcriptases is encoded by a nucleic acid that hybridizes to the complement of a nucleic acid encoding a wild type retroviral reverse transcriptases" is apparently new matter.

A careful review by the examiner of the cited pages of the specification, page 41, paragraph 0115 and page 30, paragraph 0082, failed to find any support for this limitation. There is no teaching or suggestion at the cited locations for the term "wild type" at all. Further, there is no teaching or suggestion for the limitation that the nucleic acid selected must hybridize to a "wild type retroviral reverse transcriptases"

Therefore, the new limitation represents new matter.

Response to Arguments

15. Applicant's arguments filed March 26, 2004 have been fully considered but they are not persuasive.

Claim Interpretation arguments

The first issue which Applicant addresses is that of claim interpretation. Applicant argues that it is unreasonable to interpret the term "retroviral reverse transcriptase" to encompass enzymes from bacteria such as T. aquaticus. In analyzing

the interpretation of a claim, the first question is whether the term is defined by the specification. With regard to the term "retroviral reverse transcripatase", upon which Applicant places much weight, there is no structure or definition to support that weight. The specification lists a variety of different retroviral reverse transcriptases (see pages 3 and 4), but never, in the extensive definitions section beginning at page 20, defines the term "retrovirus". The specification does indicate that Taq is a reverse transcriptase (see page 32). So the specification does not aid in the interpretation of what limitations are imposed by the term "retrovirus".

Applicant argues that the term should distinguish Taq from the claims. Applicant's basis for this argument is that Taq is an enzyme originally derived from bacteria. However, given standard molecular biological techniques, Taq can be expressed from a retrovirus. Is Taq then a "retroviral reverse transcriptase"? If so, then two tubes of identical enzymes, Taq derived from bacteria and Taq expressed by a retrovirus would be treated differently. The tube containing Taq derived from bacteria would be a "bacterial reverse transcriptase" and the tube containing Taq expressed by a retrovirus would be a "retroviral reverse transcriptase." The two tubes would be precisely identical in contents, the only difference being the label on the tube. This example shows that an ordinary artisan can interpret Taq as being structurally identical to a "retroviral reverse transcriptase" when the broadest reasonable interpretation is used. As the Federal Circuit noted in *In re Zletz* 13 USPQ2d 1320, 1322 (Fed. Cir. 1989), "During patent examination the pending claims must be interpreted as broadly as their terms reasonably allow." The Court continued "The reason is simply that during

patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed." In the current case, clarification of the scope of the language is required. The ambiguity of the term "retroviral", which is better resolved during examination than in litigation, is that the term imposes no structural limitations on the resultant enzyme, but rather serves as a source designator. Therefore, no structure is imposed by the term "wild type retroviral reverse transcriptases" since no specific structure or specific definition is given for this term in the specification. The only requirement that this term imposes is the functional requirement that the protein act as a reverse transcriptases.

112 Second paragraph arguments

Applicant then argues that the amendment to "said wild type reverse transcriptases" overcomes the indefiniteness issue because it is clear what is the reference enzyme. This argument is not found persuasive because no structure is provided for "said wild type reverse transcriptases". There are, as noted on pages 3 and 4 of the specification, many different reverse transcriptases. Again, no structural limitation is imposed by this claim language. While the relationship of the enzymes is slightly clearer, it is still uncertain what level of activity is required for the claimed enzymes. This is particularly clear due to the use of the "hybridization" language in claim 2, from which claims 16-18 and 24 depend. This hybridization language lacks any stringency requirements, so any reverse transcriptase enzyme that had a level of homology that would permit any level of hybridization, including as few as 6 or 7 contiguous shared nucleotides, would fall within the scope of the claim. This language

therefore renders the claims indefinite because it is unclear what enzyme is used for the comparison of claim 16. With the claim open to nearly any reverse transcriptase at all, the level of activity is entirely indefinite. Consequently, this rejection is maintained.

112 First paragraph arguments

Applicant reiterates the argument that the specification provides a number of examples of reverse transcriptases along with functional characteristics and guidance on the types of mutations which applicant argues provides possession of the full scope of the invention. These arguments are not persuasive because the claims lack any structural limitations on the reverse transcriptases whatsoever.

Amgen argument

When Applicant cites Amgen, Applicant is twisting this decision away from the central decisive point in the case. The Federal Circuit in Amgen stated "Thus, the undisclosed element TKT urges invalidates Amgen's product claims is a different method (endogenous activation) of making the claimed compositions. But, as the district court noted, under our precedent the patentee need only describe the invention as claimed, and need not describe an unclaimed method of making the claimed product." So in Amgen, the written description rejection was found not to apply because there were other methods of making the product, but the product itself was fully described. Here, the situation is entirely different. The product is not described. There are literally no structural requirments imposed by the claims whatsoever.

To make it absolutely clear, Applicant relies upon the conservation among retroviral reverse transcriptases. However the claim permits ANY SEQUENCE that has

reverse transcriptase activity. Since any series of mutations is permitted by this claim, one can change any "retroviral" reverse transcriptases into any other reverse transcriptases with sufficient modifications or mutations. In fact, any protein can be changed into any other protein by the appropriate selection of mutations or modifications. To the extent that pages 8 and 9 show structure, the lists of mutations are not shown by Applicant to have any beneficial effects. Finally, as noted in the rejection, claim 1 defines the reverse transcriptase solely by function. This is expressly found inadequate in Lilly to define the genus and provide possession. The current case demonstrates an instance, as in Lilly, where the absence of a precise definition of the genus, here reverse transcriptases which are modified to have certain functions, is insufficient to comply with the requirement for written description. See Id. at 1569, 43 U.S.P.Q.2d at 1405. The patentee's claims in Lilly were drawn to a large genus of all vertebrate or all mammalian insulin cDNA, while the specification of the patents only provided the cDNA sequences for the rat or human insulin proteins. See Id. at 1563, 43 U.S.P.Q.2d at 1401. Lilly held that a generic claim limitation which involved chemical formula were usually properly described. However, in the case of materials identified solely by function with chemical structure, the Federal Circuit stated that "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is." Id. at 1568, 43 U.S.P.Q.2d at 1406. Here, the definition of the reverse transcriptases operates solely on the basis of what the enzymes do, rather than what they are.

Backbone argument

When Applicant argues that other enzymes could serve as the backbone for the claimed reverse transcriptases, Applicant is arguing a limitation that is not in the claims. There is no limitation in the claims which requires any particular reverse transcriptase to serve as the backbone of the claimed enzyme. So there is no structural element imposed by the "backbone" because no "backbone" is required. None of the language in the claim provides any description of anything specific whatsoever. The claim is to an undefined genus to which an infringer not only will be uncertain if they are infringing, but more importantly, uncertain what are the bounds of the material claimed. The central aspect of patent examination is to set out clear boundaries for the public, for potential infringers and for the reviewing bodies. In this case, these claims fail to set out any bounds at all. Without any structural limitations whatsoever, the claims are not described in a manner which complies with 35 U.S.C. 112, first paragraph.

The entire discussion on page 13, in which a broad genus of enzymes that can be used as backbones is disclosed, fails to grasp the fundamental problem with the claims. No specific backbone is required. Further, no structure of a backbone is incorporated into the claim. So the claim fails to address the central point at issue in the written description analysis, which is to describe a structure correlated to a function. There are few clearer situations of the problem recognized in Lilly, "Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." The material claimed by Applicant may be capable of synthesis. However, when there are literally no structural

constraints on the material so that the ordinary practitioner not only does not know, but cannot know, what reverse transcriptases properly fall within the scope of the claims, the claims fail to meet the written description requirement.

As a final point, Applicant provides a discussion of a limited number of elements which have been found to be conserved in retroviral reverse transcriptases. None of these structural limitations are currently included in the claims. Even if they were, any single such limitation might not provide sufficient structure to overcome the written description rejection. Therefore, the written description rejection will be maintained.

Prior art Rejections

Applicant then argues that the prior art rejections are moot in view of the amendment. This is not correct based upon the claim interpretation as given above. These extremely broad claims are met by the cited prior art.

In particular, as noted in the rejection, Blain specifically teaches the delta101 mutation, which removes all the amino acids from positions 213-313, which would include the methionine at position 289 and the threonine at position 306 . Such a deletion necessarily causes a substitution at postions 289 and 306 for different amino acids, and it is unquestionably a fact that the 100% conserved regions of the MMLV reverse transcriptase would hybridize to the complement of the wild type under any level of stringency of hybridization conditions, since it is perfectly conserved with that sequence.

Applicant then argues that Arakawa does not anticipate the claim because the numbering is off. This statement is incorrect. At position 52 of the enzyme shown in the

sequence of Arakawa, there is a proline, not a leucine. So the specific enzyme of Arakawa anticipates the claim. The claim is a product claim that is not concerned with the method of making the product. The product of Arakawa clearly falls into the genus of proteins claimed by Applicant with position 52 of the disclosed sequence being a different amino acid than leucine and therefore Arakawa remains anticipatory.

Applicant reiterates the argument that Taq is not a "retroviral" reverse transcriptase. For the reasons given above, this is not persuasive.

Applicant argues that having overcome the 102 rejections, the 103 is overcome. Since the 102 rejections are all maintained, so is the 103 rejection.

All of the rejections are maintained.

Conclusion

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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